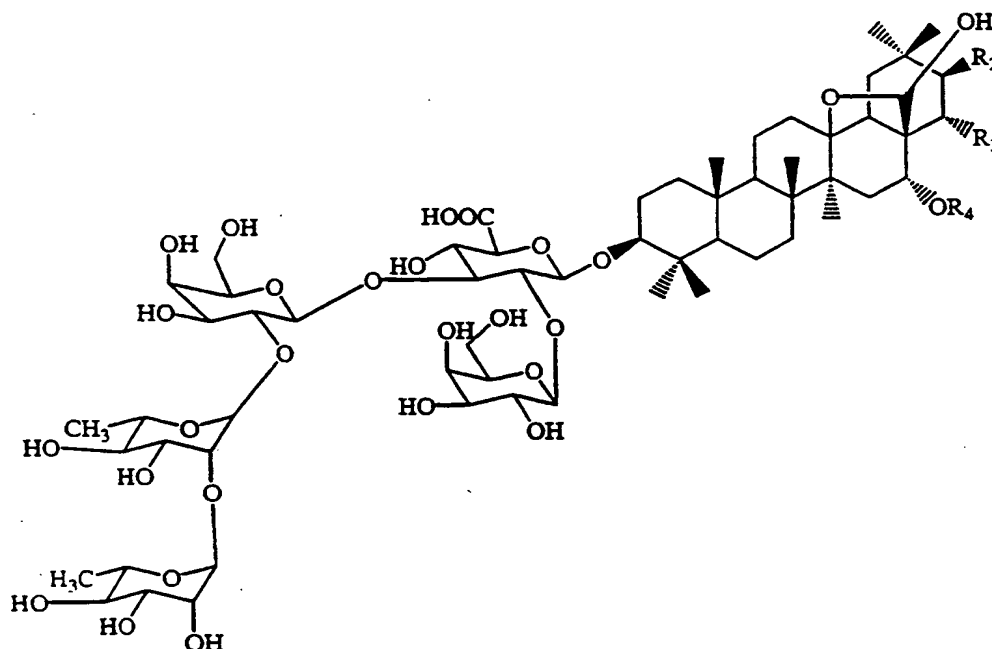


Claims

1. A process for the isolation of triterpene saponins from plants belonging to the family *Myrsinaceae*, characterized in that said process comprises the steps of
 - (a) extracting the dried plant parts with an alcohol and concentrating the extract,
 - 5 (b) removing the apolar fraction from the extract by liquid-liquid extraction with an apolar solvent, and
 - (c) further purifying the saponins in the alcohol extract by liquid -liquid extraction, filtration and chromatography.
- 10 2. A process according to claim 1 wherein the alcohol is methanol, ethanol, isopropanol, butanol, each optionally admixed with water.
3. A process according to claim 1 wherein the saponins of the alcohol extract are further purified by
 - 15 (c6) extracting the aqueous fraction with butanol saturated with water,
 - (c7) evaporating the organic layer to dryness,
 - (c8) washing the residue in a ketone, and
 - (c9) filtering off the crude saponin mixture.
- 20 4. A process according to claim 1 wherein the saponins are isolated from the plant species *Maesa balansae*, and the chromatography comprises straight phase chromatographyliquid chromatography on silicagel or reversed-phase liquid chromatography with gradient eluent system using
 - A : 0.5 % ammonium acetate in water
 - 25 B : methanol
 - C : acetonitrilewherein at $t = 0$, $(A:B:C) = (60:20:20)$ and $t = \text{end}$, $(A:B:C) = (0:50:50)$.
- 30 5. A triterpene saponin obtainable by a process according to anyone of claims 1 to 4.
6. A triterpene saponin according to claim 5 wherein said saponin is isolated from the plant species *Maesa balansae*, and the chromatography comprises reversed-phase liquid chromatography with gradient eluent system using
 - A : 0.5 % ammonium acetate in water
 - 35 B : methanol
 - C : acetonitrilewherein at $t = 0$, $(A:B:C) = (60:20:20)$ and $t = \text{end}$, $(A:B:C) = (0:50:50)$, and wherein said saponin has the following characteristics :

- Compound 1 : MW = 1532, λ_{\max} = 228.6 nm, $\lambda_{\max 2}$ = 273.3 nm ;
 Compound 2 : MW = 1510, λ_{\max} = 223.9 nm, $\lambda_{\max 2}$ = 274.5 nm ;
 Compound 3 : MW = 1532, λ_{\max} = 279.2 nm, $\lambda_{\max 2}$ = 223.9 nm ;
 Compound 4 : MW = 1510, λ_{\max} = 280.4 nm, $\lambda_{\max 2}$ = 222.7 nm ;
 5 Compound 5 : MW = 1574, λ_{\max} = 276.8 nm, $\lambda_{\max 2}$ = 225.0 nm ; or
 Compound 6 : MW = 1552, λ_{\max} = 279.2 nm, $\lambda_{\max 2}$ = 223.9 nm.

7. A triterpene saponin having the formula



- 10 wherein R_2 is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ or $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,
 R_3 is (E) or (Z) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$, and
 R_4 is hydrogen or $-(\text{C}=\text{O})\text{CH}_3$.

8. A compound according to claim 7 wherein
 15 in compound 1, R_2 is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,
 R_3 is (Z) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$,
 R_4 is hydrogen;
 in compound 2, R_2 is $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,
 R_3 is (Z) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$,
 R_4 is hydrogen;
 20 in compound 3, R_2 is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,
 R_3 is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$,
 R_4 is hydrogen;

in compound 4, R_2 is $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,
 R_3 is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$,
 R_4 is hydrogen;

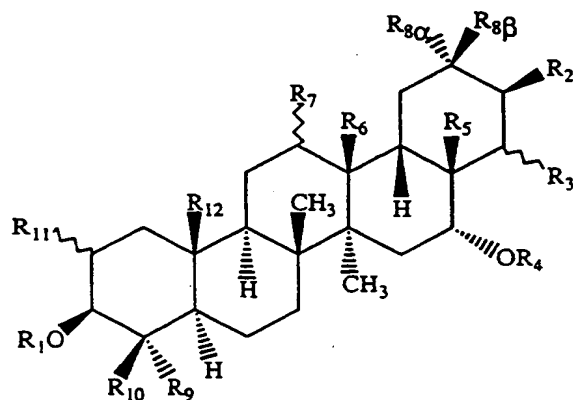
in compound 5, R_2 is $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,
 R_3 is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$,
 R_4 is $-(\text{C}=\text{O})\text{CH}_3$;

in compound 6, R_2 is $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$,
 R_3 is (E) $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$,
 R_4 is $-(\text{C}=\text{O})\text{CH}_3$.

9. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and as an active ingredient a triterpene saponin as defined in claim 5, 6, 7 or 8.

10. A composition according to claim 7 adapted for parenteral administration.

11. Use of one or more triterpene saponins for the preparation of a pharmaceutical composition for treating leishmaniasis in hosts infected by *Leishmania* species, characterized in that the saponin has the formula



a stereoisomeric form thereof or a pharmaceutically acceptable addition salt thereof, wherein

R_1 is hydrogen, $-(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$, $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ substituted with phenyl, a monosaccharide group or an oligosaccharide group ;

R_2 is hydrogen, hydroxy, $-\text{O}(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$, or $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ substituted with phenyl ;

R_3 is hydrogen, hydroxy, $-\text{O}(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$, or $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ substituted with phenyl ;

R_4 is hydrogen, $\text{C}_{1-6}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$, $-(\text{C}=\text{O})\text{C}_6\text{H}_5$, or $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ substituted with phenyl ;

R₅ is CH₃, CH₂OH, CH₂OCH₃, CH₂O-C(=O)CH₃, CHO, COOH ; or

R₅ and R₂ form a divalent radical of formula -C(=O)-O- ;

R₆ and R₇ are hydrogen; or taken together they form a bond; or

R₅ and R₆ form a divalent radical of formula

5 -CH₂-O- (a),

 -CH(OR₁₃)-O- (b),

 -C(=O)-O- (c),

 wherein R₁₃ is hydrogen, C₁₋₆alkyl or -(C=O)C₁₋₅alkyl ;

R_{8α} and R_{8β} each independently represent CH₃, CH₂OH, CH₂OCH₃,

10 CH₂O-C(=O) C₁₋₅alkyl, CHO, CH(OCH₃)₂, CH=NOH, COOH ;

 R_{8β} and R₃ form a divalent radical of formula -C(=O)-O- ;

R_{8β} and R₅ form a divalent radical of formula -CH₂O-CHOH- ;

R₉ is CH₃, CH₂OH, CH₂OCH₃, CH₂O-C(=O)C₁₋₅alkyl, CHO, COOH ;

R₁₀ is CH₃, CH₂OH, CH₂OCH₃, CH₂O-C(=O)C₁₋₅alkyl, CHO, COOH ;

15 R₁₁ is hydrogen, hydroxy or O-C(=O)C₁₋₅alkyl ; or R₁₀ and R₁₁ form a divalent
 radical of formula -CH₂O- ; and

R₁₂ is CH₃, CH₂OH, CH₂OCH₃, CH₂O-C(=O)CH₃, CHO, CH=NOH, or COOH.

12. Use according to claim 11 wherein

20 R₁ is hydrogen, -(C=O)C₁₋₅alkyl, or an oligosaccharide group ;

R₃ is hydrogen, hydroxy, -O(C=O)C₁₋₅alkyl, -O(C=O)C₂₋₅alkenyl,
 -O(C=O)C₂₋₅alkenyl substituted with phenyl ;

R₄ is hydrogen, C₁₋₆alkyl, -(C=O)C₁₋₅alkyl, -(C=O)C₂₋₅alkenyl ;

R₅ is CH₂OH, CH₂O-C(=O)CH₃, CHO ; and

25 R₆ and R₇ taken together form a bond; or

R₅ and R₆ form a divalent radical of formula

 -CH₂-O- (a),

 -CH(OR₁₃)-O- (b),

 -C(=O)-O- (c),

30 wherein R₁₃ is hydrogen, C₁₋₆alkyl or -(C=O)C₁₋₅alkyl, ; and

R₇ is hydrogen ;

R_{8β} represents CH₃, CH₂OH, CHO, CH(OCH₃)₂, CH=NOH, COOH ;

R_{8α} represents CH₃ ;

R_{8β} and R₃ form a divalent radical of formula -C(=O)-O- ; or

35 R_{8β} and R₅ form a divalent radical of formula -CH₂O-CHOH- ;

R₁₀ is CH₃, CH₂OH ;

R₁₁ is hydrogen, hydroxy or O-C(=O)C₁₋₅alkyl ; or

R_{10} and R_{11} form a divalent radical of formula $-\text{CH}_2\text{O}-$; and
 R_{12} is CH_3 , CH_2OH , $\text{CH}_2\text{O}-\text{C}(=\text{O})\text{CH}_3$, CHO , or $\text{CH}=\text{NOH}$.

13. Use according to claim 12 wherein

5 R_1 is hydrogen or an oligosaccharide group ;

R_2 is hydrogen, hydroxy, $-\text{O}(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$,
 or $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ substituted with phenyl ;

R_3 is hydrogen, hydroxy, $-\text{O}(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$,
 $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ substituted with phenyl ;

10 R_4 is hydrogen, $\text{C}_{1-6}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$, $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$, $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$
 substituted with phenyl ;

R_5 is CH_2OH , CH_2OCH_3 , $\text{CH}_2\text{O}-\text{C}(=\text{O})\text{CH}_3$, CHO , COOH ; and

R_6 and R_7 taken together form a bond; or

R_5 and R_6 form a divalent radical of formula

15 $-\text{CH}_2-\text{O}-$ (a),

$-\text{CH}(\text{OR}_{13})-\text{O}-$ (b),

$-\text{C}(=\text{O})-\text{O}-$ (c),

wherein R_{13} is hydrogen ; and

R_7 is hydrogen ;

20 $R_{8\alpha}$ and $R_{8\beta}$ both represent CH_3 ;

R_9 is CH_3 ;

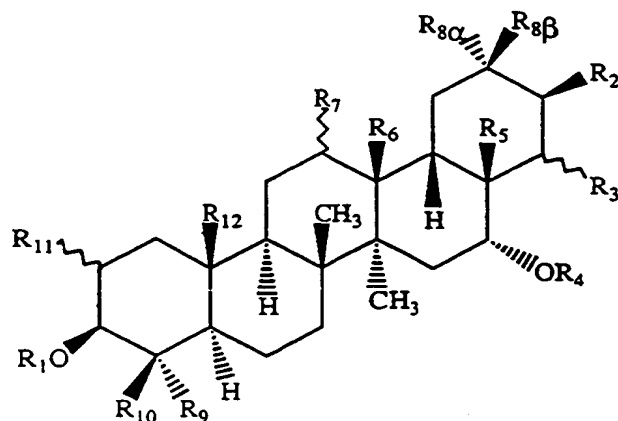
R_{10} is CH_3 ;

R_{11} is hydrogen ; and

R_{12} is CH_3 .

25

14. A method of alleviating clinical manifestations of, and curing disorders known as leishmaniases attributable to infection by protozoan parasites of the genus *Leishmania* in both men and animals, comprising administering to an infected host a therapeutically effective amount of a compound of formula:



a stereoisomeric form thereof or a pharmaceutically acceptable addition salt thereof, wherein

R_1 is hydrogen, $-(C=O)C_{1-5}alkyl$, $-(C=O)C_{2-5}alkenyl$, $-(C=O)C_{2-5}alkenyl$ substituted with phenyl, a monosaccharide group or an oligosaccharide group ;

R_2 is hydrogen, hydroxy, $-O(C=O)C_{1-5}alkyl$, $-O(C=O)C_{2-5}alkenyl$, $-O(C=O)C_6H_5$, or $-O(C=O)C_{2-5}alkenyl$ substituted with phenyl ;

R_3 is hydrogen, hydroxy, $-O(C=O)C_{1-5}alkyl$, $-O(C=O)C_{2-5}alkenyl$, $-O(C=O)C_6H_5$, or $-O(C=O)C_{2-5}alkenyl$ substituted with phenyl ;

R_4 is hydrogen, $C_{1-6}alkyl$, $-(C=O)C_{1-5}alkyl$, $-(C=O)C_{2-5}alkenyl$, $-(C=O)C_6H_5$, or $-(C=O)C_{2-5}alkenyl$ substituted with phenyl ;

R_5 is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)CH_3$, CHO , $COOH$; or

R_5 and R_2 form a divalent radical of formula $-C(=O)-O-$;

R_6 and R_7 are hydrogen; or taken together they form a bond; or

R_5 and R_6 form a divalent radical of formula

$-CH_2-O-$ (a),

$-CH(OR_{13})-O-$ (b),

$-C(=O)-O-$ (c),

wherein R_{13} is hydrogen, $C_{1-6}alkyl$ or $-(C=O)C_{1-5}alkyl$;

$R_{8\alpha}$ and $R_{8\beta}$ each independently represent CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)C_{1-5}alkyl$, CHO , $CH(OCH_3)_2$, $CH=NOH$, $COOH$;

$R_{8\beta}$ and R_3 form a divalent radical of formula $-C(=O)-O-$;

$R_{8\beta}$ and R_5 form a divalent radical of formula $-CH_2O-CHOH-$;

R_9 is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)C_{1-5}alkyl$, CHO , $COOH$;

R_{10} is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)C_{1-5}alkyl$, CHO , $COOH$;

R_{11} is hydrogen, hydroxy or $O-C(=O)C_{1-5}alkyl$; or R_{10} and R_{11} form a divalent radical of formula $-CH_2O-$; and

R_{12} is CH_3 , CH_2OH , CH_2OCH_3 , $CH_2O-C(=O)CH_3$, CHO , $CH=NOH$, or $COOH$.